OPTICAL-FIBER TYPE VITAL LIVER FUNCTION SENSOR AND EXAMINATION DEVICE

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Inventor(s): SUSAKA AKIO; SASAKI KAZUMASA; FUJITA SHOICHI; KATO MIE
Applicant(s): SASAKI KAZUMASA; SUSAKA AKIO
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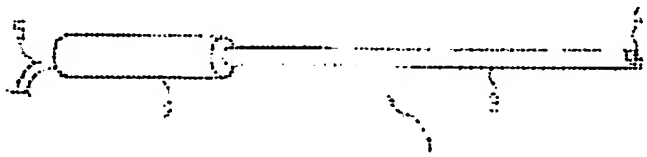
Abstract of **JP 9276275 (A)**

PROBLEM TO BE SOLVED: To provide a new detecting method that is directly applicable to vital liver and has high accuracy, for detecting cytochrome P450 enzyme or lipid peroxide, and to provide a device therefor. SOLUTION: In a vital liver function examining device, which detects the activity of chemical metabolic enzyme cytochrome P450 and the amount of lipid peroxide produced in living liver, the characteristics of the enzyme and lipid peroxide that they are sensitive to light with specific wavelengths are utilized in such a way that illuminating light is introduced through an optical fiber 4 mounted in a capillary 3 whose end is cut diagonally, and the light reflected or scattered from or transmitted through either the enzyme. a liquid containing the enzyme, a substance produced by the reaction of another chemical with the enzyme, or the lipid peroxide, or fluorescence induced in those materials by the illuminating light, is taken out of the living body through the optical fiber 4 or another optical fiber. From this optical signal obtained, the activity of the enzyme or the amount of lipid peroxide produced can be measured.



* NOTICES *

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CLAIMS

[Claim(s)]
[Claim 1]In a living body liver function test device which detects the activity of the drug-metabolizing enzyme cytochrome P450 within living body liver, and a generated amount of peroxylipid, It uses that this enzyme and peroxylipid have the induction characteristic to light of specific wavelength, Irradiation light is made to introduce through an optical fiber attached in a small tube which cut a tip aslant and formed it, Catoptric light, the scattered light, the transmitted lights, or these substances from a substance by which it was generated by a reaction with a fluid, or other drugs and this enzyme containing this enzyme or this enzyme, or peroxylipid fluorescence induced by irradiation light, An optical fiber form living body liver function sensor characterized by taking out out of a living body by the same optical fiber or other optical fibers, and enabling it to measure the activity of this enzyme, or a generated amount of peroxylipid from this acquired lightwave signal.
[Claim 2]In a small tube inserted in living body liver, a movable piece is built in an optical fiber and parallel, And a mirror plane is formed so that a tip may be cut at an angle which is 45 degrees and an apical surface of an optical fiber may reflect light, By turning at irradiation light from light equipment vertically to an axis of an optical fiber, being ejected from a wall surface of an optical fiber, hitting a wall surface of a small tube and reflecting it, By retreating a movable piece which it is made to return to this optical fiber again, and was provided in a small tube tip part, a blank of a predetermined interval is formed in a small tube, and a constant rate of living body liquid is incorporated into this opening, The optical fiber form living body liver function sensor according to claim 1, wherein irradiation light which carries out both-way passage of there enables it to quantify this enzyme or the light-sensitive nature of peroxylipid correctly.
[Claim 3]As for an optical fiber in a small tube inserted in living body liver, a tip is cut by an acute angle of 45 degrees or less, And are a mirror plane so that an apical surface may be reflected, and bend in a transverse direction, reflect in a wall surface of a small tube, and irradiation light from light equipment is irradiated aslant, The optical fiber form living body liver function sensor according to claim 1, wherein this optical fiber enables it to supplement only with fluorescence newly generated without incorporating catoptric light from a wall surface of a small tube efficiently.
[Claim 4]By building a small tube for drug solution introduction in a small tube inserted in living body liver with an optical fiber, making drugs pour in with the small tube, and making it react to this enzyme or peroxylipid, Claim 1 raising optical perception sensitivity and the optical fiber form living body liver function sensor according to claim 2.
[Claim 5]A living body liver function test device which comprises chemical dosing equipment, comprising:
An optical fiber form living body liver function sensor.
Light equipment which consists of a light source for absorption measurement, and a light source for fluorometry.
A wavelength analyzer which analyzes luminous intensity introduced from the above-mentioned sensor.
A computer and a chemicals feed pump which calculate and ask for enzyme cytochrome P450 or peroxylipid's existence concentration.

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the test equipment which can perform the inspection of a vital function without taking out the piece of an organ in living body liver, and the optical fiber form living body liver function sensor for it.
[0002]
[Description of the Prior Art]In order to inspect a hepatic function certainly conventionally, it was carrying out by taking out the piece of an organ in liver other than a blood test. For this reason, the large-scale operation for an inspection, etc. are needed. It is known that it will be regarded as the enzyme cytochrome P450 which exists in living body liver playing the role important for oncogenesis recently, and the existence will increase peroxylipid with an impaired liver function, oncogenesis, aging, etc. It is expected very much that measuring this quantitatively opens the new side to the medical examination of a hepatic function.
[0003]By the way, in order to have conducted such an inspection, the piece of liver was extracted from in the living body, the chemical treatment of this was carried out, measured by the chemical analysis, the inspection by the photoreaction was conducted, and also there was no method. In such an inspection method, the taken-out piece of liver was in the state where living body activity was suspended, the inspection by the reaction under living body activity is difficult, and the limit had produced it in research or diagnosis.
[0004]
[Problem(s) to be Solved by the Invention]Then, the knowledge of there being sensitivity in this invention to the light of wavelength with specific research result, enzyme CHITOROMU P450, or peroxylipid of **** of these artificers is acquired, By making the light of the specific wavelength which serves as a light source by an optical fiber introduce in the living body, irradiating with analyte, and taking out again the light which the reply signal contained out of a living body by an optical fiber, It traced that a means by which actions, such as existence of the enzyme cytochrome P450 in the living body or generation of peroxylipid, and disappearance, can be certainly observed in real time without seldom affecting living body activity was obtained.
[0005]If the abundance of the enzyme cytochrome P450 changes within living body liver, it will be thought that it leads to change of a living body's hormone level, the increase in the rate of cancerogenesis, and the increase in peroxylipid. Therefore, early detection of such change becomes very important on a healthy medical checkup. An appearance of the measuring device with high accuracy which can be used for diagnosis, therapy progress pursuit, and therapy research until now was desired. However, under the present circumstances, the device which can be used for diagnosis is not developed. This invention was made in view of such a point, and can be directly applied to a living body, and it aims at moreover providing cytochrome P450 high-precision enzyme or the new detecting method of peroxylipid, and the device for it.
[0006]
[Means for Solving the Problem]In a living body liver function test device with which this invention measures activity and a peroxylipid generated amount of the enzyme cytochrome P450 within living body liver, It uses that this enzyme and peroxylipid have the induction characteristic to light of respectively specific wavelength, Irradiation light is made to introduce through an optical fiber which attached a tip in a small tube cut aslant, Catoptric light, the scattered light, the transmitted lights, or these substances from a substance by which it was generated by a reaction with a fluid, other drugs and this enzyme, or peroxylipid containing this enzyme or this enzyme fluorescence induced by irradiation light, It is an optical fiber form living body liver function sensor characterized by taking out out of a living body by the same optical fiber

or other optical fibers, and enabling it to identify an yield of this enzyme or peroxylipid from this acquired lightwave signal. An optical fiber in a small tube inserted in living body liver, A mirror plane is formed so that a tip may be cut at an angle which is 45 degrees and an apical surface may reflect light, Bend vertically to an axis of an optical fiber, and it is ejected from a wall surface of an optical fiber, hit and reflect in a wall surface of the other side of a small tube, and irradiation light from light equipment is introduced into this optical fiber, by retreating a movable piece provided in an inside of a small tube, a blank of a predetermined interval is formed in a small tube, and a constant rate of living body liquid is incorporated into this opening, [crowd and] Irradiation light which carries out both-way passage of there is the optical fiber form living body liver function sensor which enabled it to quantify this enzyme or the light-sensitive nature of peroxylipid correctly.

[0007]Furthermore an optical fiber in a small tube which inserts this invention in living body liver, It is a mirror plane so that a tip may be cut by an acute angle of 45 degrees or less and it may reflect by an apical surface, Bend in a transverse direction, reflect in a wall surface of a small tube, and irradiation light from light equipment is irradiated aslant, This optical fiber is the optical fiber form living body liver function sensor which enabled it to supplement only with fluorescence newly generated without incorporating catoptric light from a wall surface of a small tube efficiently, It is the optical fiber form living body liver function sensor which raised optical perception sensitivity by building a small tube for drug solution introduction in a small tube inserted in living body liver with an optical fiber, making drugs pour in with the small tube, and making it react to this enzyme substance.

[0008]A living body liver function test device this invention is characterized by that comprises the following and which comprises chemical dosing equipment.

Optical fiber form living body liver function sensor.

Light equipment which consists of a light source for absorption measurement, and a light source for fluorometry.

A wavelength analyzer which analyzes luminous intensity introduced from the above-mentioned sensor.

A computer and a chemicals feed pump which calculate and ask for enzyme cytochrome P450 and peroxylipid's existence concentration.

[0009]

[Embodiment of the Invention]This invention the enzyme cytochrome P450 and peroxylipid which are generated in a specific organ in the living body, for example, liver, Without taking out the piece of liver, irradiation light is led to the inside of liver using the sensor which consists of optical fibers, and it is related with the test equipment which analyzes the optical fiber form living body liver function sensor which detects this enzyme and peroxylipid using the photoreaction, and its signal. Therefore, the tip part of stainless steel or the small tube made from plastics (catheter) is cut aslant, and is formed so that a difference may be directly carried out to an organ and it may be loaded, and an optical fiber is stored inside this small tube, and it is constituted. A tip is acutely cut in the shape of a hypodermic needle, the tip of a small tube is formed so that it can insert directly easily for a living body, and the thickness is 0.2mm-5mmphi.

[0010]Hereafter, based on a drawing, the example of this invention is described in detail. The perspective view in which drawing 1 shows the composition of one example of an optical fiber form living body liver function sensor, and drawing 2 are the perspective views showing a part of grasping part. That is, the optical fiber form living body liver function sensor 1 comprises the small tube (catheter) 3 mainly attached to the grasping part 2 and this grasping part 2. Into this small tube 3, the optical fiber 4 about thickness [of 0.05-0.2 mm] phi is inserted, and the same as that of the inside diameter of the small tube 3 or it is smaller than it. When, when the optical fiber 4 is thinner than the inside diameter of the small tube 3, the optical fiber 4 is pasted up, and it is fixed to one side of the wall of the small tube 3. It is connected with the connecting optical fiber 5 through the grasping part 2, and this optical fiber 4 is connected with the external light equipment and the wavelength analyzer which are not illustrated. The jig mounting part 6 for attaching the connecting optical fiber 5 and a jig is formed in the grasping part 2.

[0011]The tip part of the above-mentioned small tube 3 is cut and formed aslant [hypodermic needle-shaped], in order to insert in the living body, as shown in the enlarged drawing of the tip end part of drawing 3. In the case of this example, it is possible for the optical fiber 4 to be embedded and constituted and to form the whole inside diameter of the small tube 3 so thinly. Therefore, as shown in the sectional view of drawing 4, the irradiation light 9 from the optical fiber 4 shines upon the object 7 which is approaching through the space where it is refracted by a slanting tip part, and living body liquid is filled, and is scattered about or reflected. At this time, between the object 7 and the small tubes 3 is the inspected

field 8, and if the enzyme cytochrome P450 or peroxylipid exists in this inspected field 8 by the irradiation light 9, the scattered light or the catoptric light 10 will arise, This enters into the optical fiber 4 in the small tube 3 again, and is drawn in the sensing device which is not illustrated with the connecting optical fiber 5 through the grasping part 2.

[0012]Since only the ingredient of a specified wavelength will receive absorption strongly among the irradiation light 9 from the optical fiber 4 if the enzyme cytochrome P450 or peroxylipid exists in the living body liquid in the inspected field 8 at this time, this wavelength component shows bigger attenuation than other wavelength components among irradiation light. It is possible to judge the existence or nonexistence of the enzyme cytochrome P450 or peroxylipid from this information.

[0013]In the case of this example, since the distance to the dispersion object 7 is indefinite, it is unsuitable for quantitive measurement. Since the fluorescence of a specified wavelength occurs by pouring in a specific reaction reagent when the enzyme cytochrome P450 or peroxylipid which exists in the inspected field 8 is little, sharp measurement is attained by supplementing with this by the optical fiber 4, and measuring it.

[0014]The perspective view and drawing 6 which drawing 5 shows the sensor-tips part which shows the 2nd example are a sectional view. That is, like the previous example, the tip part of the optical fiber form living body liver function sensor 1 is cut aslant, and is formed. In the small tube 3a of this sensor 1, the optical fiber 4 is inserted, and the mirror plane 12 is established at that tip, and the movable piece 11 of the slant face formed in the shape of a semicircular pillar so that a half might touch the inside diameter of the small tube 3a mostly is inserted and constituted. Therefore, after inserting the movable piece 11 in the living body, by lengthening the movable piece final controlling element of the grasping part 2 which is not illustrated, the movable piece 11 is retreated in the direction of arrow A, and a blank is formed. Thereby, the inspected field 8 is formed in the small tube 3a. It is reflected in the mirror plane 12, and the irradiation light 9 is ejected horizontally and reflected on the wall surface of the small tube 3a. Therefore, since only the ingredient of a specified wavelength will receive absorption strongly among the irradiation light 9 from the optical fiber 4 if it irradiates with the living body liquid in the inspected field 8 and the enzyme cytochrome P450 or peroxylipid exists in the living body liquid in this inspected field 8, This wavelength component shows bigger attenuation than other wavelength components among irradiation light. It is possible to judge the existence or nonexistence of the enzyme cytochrome P450 or peroxylipid from this information, and since it is very good, strong catoptric light is obtained, and the reflection efficiency in the inner surface of the small tube 3a becomes effective in improvement in the S/N ratio of a signal.

[0015]Drawing 7 is a perspective view showing the sensor-tips part which shows the 3rd example. That is, the tip part of the optical fiber form living body liver function sensor 1 is cut acutely, and is formed aslant. Into the small tube 3b of this sensor 1, the lead pipe 13 which can pour in the optical fiber 4 and drugs is inserted, and it is constituted. As the irradiation light 9 of the specified wavelength belt from light equipment is shown in the sectional view of drawing 8, total internal reflection happens on the boundary of optical fiber glass and a fluid with a high refractive index. It reflects by the tip part of this optical fiber 4, it reflects in the reflector 14 further established in the small tube 3b, and irradiates with the inspected field 8 from an oblique direction. If the enzyme cytochrome P450 or peroxylipid exists in this inspected field 8, fluorescence 10' will arise, and it enters into the optical fiber 4 almost linearly again, and is supplemented in the optical fiber 4, and this fluorescence 10' is drawn in the sensing device which is not illustrated through the grasping part 2, and is measured. The lead pipe 13 is for pouring a drug solution into the inspected field 8, as shown in the arrow B.

[0016]Although what inserts one optical fiber which ejects irradiation light into a small tube in each example mentioned above, and performs introductory light from an inspected field by the same optical fiber was explained, Two of these are inserted into a small tube, and, naturally it is good also considering the optical fiber of irradiation light, and the optical fiber of an introductory light as another optical fiber.

[0017]Next, the composition and the inspection method of a device are explained based on drawing 10 in which the composition of drawing 9 and light equipment which are the general drawing of test equipment is shown. That is, the chemical supply pipe 32 is connected with the connecting optical fiber 5 at the grasping part 2 of the optical fiber form living body liver function sensor 1 inserted in the living body 35. The above-mentioned chemical supply pipe 32 is connected to the drugs bottle 34 via the chemicals feed pump 33. On the other hand, the connecting optical fiber 5 is connected to the light equipment 21 and the wavelength analyzer 30 via the coupler 29. And this wavelength analyzer 30 is connected with the computer 31.

[0018]The above-mentioned light equipment 21 has the two connectors, the light source 24 for absorption measurement, and the fluorescence source 25, A and B. First, in absorption measurement, the connecting optical fiber 5 of the optical fiber form living body liver function sensor 1 is connected to the terminal A via

the coupler 29. The light source of the wavelength range the enzyme cytochrome P450 or near the absorption wavelength of peroxylipid is connected to this terminal A. As this light source, a halogen tungsten lamp, a xenon lamp, a mercury lamp, and laser can be used. Drawing 10 shows the light equipment 21 in the case of using two sets of laser, and after it mixes the helium neon laser 25 which oscillates the light of the wavelength which is not absorbed as the argon laser 24 near absorption center wavelength, and a reference beam with the optical coupler 26, it has connected it to the terminal A.

[0019]In carrying out fluorometry, it connects the connecting optical fiber 5 of the optical fiber form living body liver function sensor 1 to the terminal B of the light equipment 21 via the coupler 29. In order to use the fluorescence of the enzyme cytochrome P450 or peroxylipid as this light source 28, the mercury lamp, carbon arc lamp, or xenon lamp containing many lights of 300-500 nm of wavelength ranges is used.

[0020]The light taken out from the light equipment 21 with the connecting optical fiber 5 is connected to the grasping part 2 of the optical fiber form living body liver function sensor 1 by the coupler 29 with the lead pipe 32. The coupler 29 connects illuminant light to the optical fiber 5, and it has connected optical fiber 5' which separates the reversing optical signal and is led to the wavelength analyzer 30.

[0021]In absorption measurement, as shown in drawing 4 and drawing 6, the irradiation light 9 is emitted from the tip part of the optical fiber form living body liver function sensor 1, and it supplements with the scattered light or the catoptric light 10. In fluorometry, as shown in drawing 8, the irradiation light 9 is emitted from the tip part of the optical fiber form living body liver function sensor 1, and it supplements with fluorescence 10'. And as for an optical signal, both are led to the wavelength analyzer 30 via the optical fiber 4, the connecting optical fiber 5, and optical fiber 5', and light intensity is measured.

[0022]The wavelength analyzer 30 measures the light intensity in each wavelength. Absorption of the enzyme cytochrome P450 or peroxylipid or the quantity of fluorescence is calculated using the computer 31 from the value, and it asks for the enzyme cytochrome P450, the existence or nonexistence of peroxylipid, or existence concentration from these information further. The result is printed by the display for indication or recorder of the computer 31, and can diagnose now immediately.

[0023]Next, the method of the fixed-quantity measurement by absorption is explained in detail. The quantity of the light which makes power of the irradiation light from a light source I_0 (lambda 1), and can detect it if the medium which the light of the wavelength lambda 1 penetrates has absorption and the absorptivity will be set to alpha (lambda 1) is $I(\lambda 1) = I_0(\lambda 1) T^2 \exp(-\alpha(\lambda 1) x$... (1)

There is ******. Here, as for the light path length in a medium, and T, the transmissibility of the optical fiber 4, the optical fiber 5, and optical fiber 5' and P of x are the reflective recovering efficiency of the optical fiber form living body liver function sensor 1.

[0024]On the other hand, and it is $I(\lambda 2) = I_0(\lambda 2) T^2 P$... (2) [wavelength component lambda_2 which is not absorbed]

It comes out. T^2P is $I(\lambda 1) = I_0(\lambda 1) [I(\lambda 2)/I_0(\lambda 2)]$ and exp-alpha (lambda 1) x, when it considers that it is common also in (1) type, (2) types are transformed and it substitutes to (1) type, since it is not dependent on wavelength... (3)

A next door, therefore $\alpha(\lambda 1) = -(1/x) \ln [I(\lambda 1) I_0(\lambda 2) / I_0(\lambda 1) I(\lambda 2)]$ ... (4)

It becomes. Since alpha is generally proportional to the concentration C by the linearity medium of which the D'Alembert rule consists, it makes Q a constant, and it is $C = -Q \ln [I(\lambda 1) I_0(\lambda 2) / I_0(\lambda 1) I(\lambda 2)]$.

... (5)

It can set. Concentration will be decided if it substitutes for the above-mentioned (5) formula in quest of ratio $I(\lambda 1)/I_0(\lambda 1)$ and $I(\lambda 2)/I_0(\lambda 2)$ using the light intensity in lambda 1 measured with the wavelength analyzer 30, and lambda 2. However, it is necessary to search for an analytical curve using the sample of the known concentration C beforehand. Q is inclination of an analytical curve.

[0025]When distribution of an optical path is constant, a measuring value serves as a straight line to concentration like drawing 12, and inclination of a measuring value is called for by measurement of two points. However, the length of an optical path changes small [every] with angles of radiation of a beam of light, and there is intensity distribution also in light so that the structure of the sensor shown in the 2nd example (refer to drawing 6) may show the optical fiber form living body liver function sensor 1 of this invention. In such a case, an analytical curve may not turn into a straight line, as shown in drawing 13. Therefore, the highly precise measurement of an analytical curve is attained by asking from a plotting point as mostly as possible.

[0026]The device of the example shown in drawing 9 is mainly a device aiming at the object for research, and its economic burden is large for installing in medical inspection organizations, such as each hospital. Then, an indispensable portion is integrated and the facilitated example is shown in drawing 11. That is, 29' is an integration optical coupler and has a function equivalent to the optical coupler 29 of a previous example. The bandpass form light wavelength filter 36 is connected to this optical coupler 29', only the light of specific wavelength is taken out by this and the optical signal which has returned from the sensor part 1 via the optical fiber 5 is changed into an electrical signal by the photodetector 37. 28' is the laser of the excitation light source. It is connected to the signal generator 40 and this is modulated by the signal of a certain frequency generated from here. Since noise is mixed, this signal has noise removed by the lock in amplifier 38 although this modulated wave form is taken over also to the signal wave form from the photodetector of 37. As a synchronized signal of the lock in amplifier 38, the signal of the signal generator 40 used for abnormal conditions with the wiring 42 is added. 41 makes an optical system section an integrated optic circuit, and when a lightwave signal is weak, the amplifier 42 is installed in an optical circuit.

[0027]

[Effect of the Invention]According to the optical fiber form living body liver function sensor and test equipment of this invention, it is possible within living body liver to detect the existence or nonexistence and existence concentration of the enzyme cytochrome P450 or peroxylipid with high precision, and it can use for a healthy medical checkup, or therapy progress pursuit and therapy research as explained above.

[Translation done.]